Supporting Information

Free Energy Landscape of Lipid Interactions with Regulatory Binding Sites on the Transmembrane Domain of the EGF Receptor

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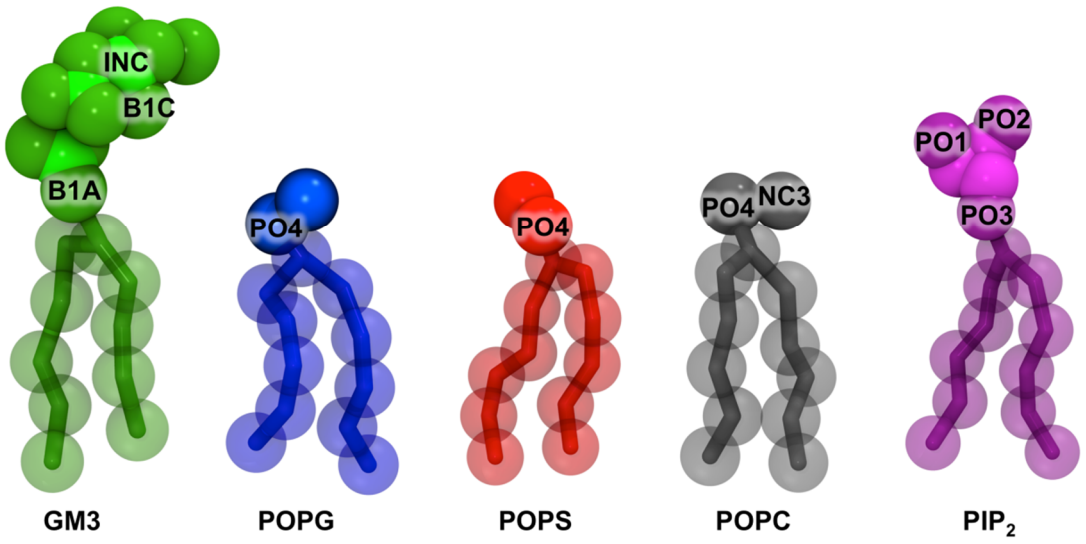

Figure S1. CG lipids used in simulations and relevant bead names. CG lipids used in simulations and relevant CG bead types. B1C, PO4, and PO3 each bear a formal charge of -1, whilst PO1 and PO2 each bear a formal charge of -2, and NC3 a charge of +1. The POPG, POPC, and POPS lipids utilized in simulations were as described in the MARTINI forcefield, whilst the glycolipid GM3 and the phosphoinositide PIP_2 were described using locally developed versions (see main text for details).

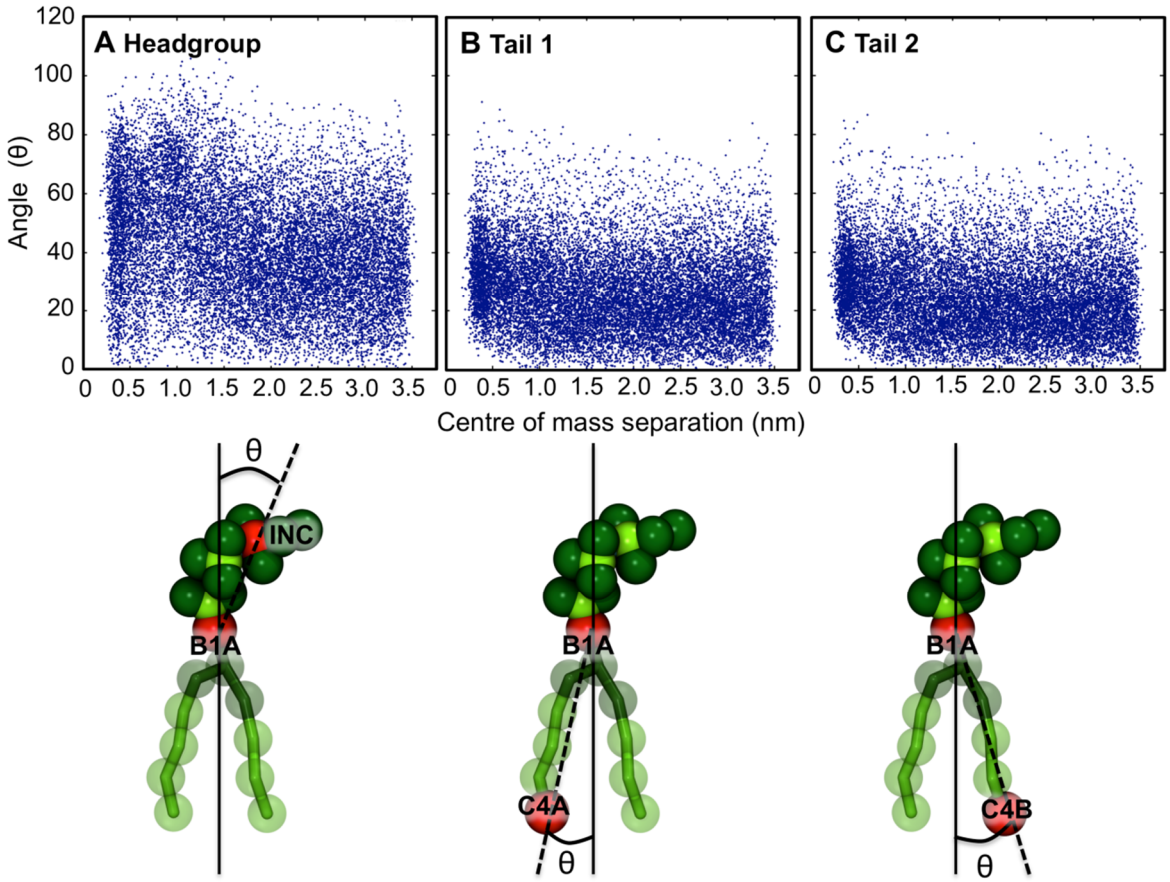

Figure S2. Relationship between GM3 tilt angle and protein proximity. GM3 "tilts" relative to the membrane normal to form optimal interactions with the N-termini of the transmembrane helix dimer. (A) Distribution of headgroup angles over the reaction coordinate sampled during PMF calculations. (B+C) Angle distributions for tail 1 and tail 2. Beneath each plot is a cartoon depicting the angle reported. In each case a vector was drawn between the two beads indicated in red, and the angle between this line and the membrane normal measured for each frame of a concatenated trajectory of all window used during calculation of the GM3 PMF profile.

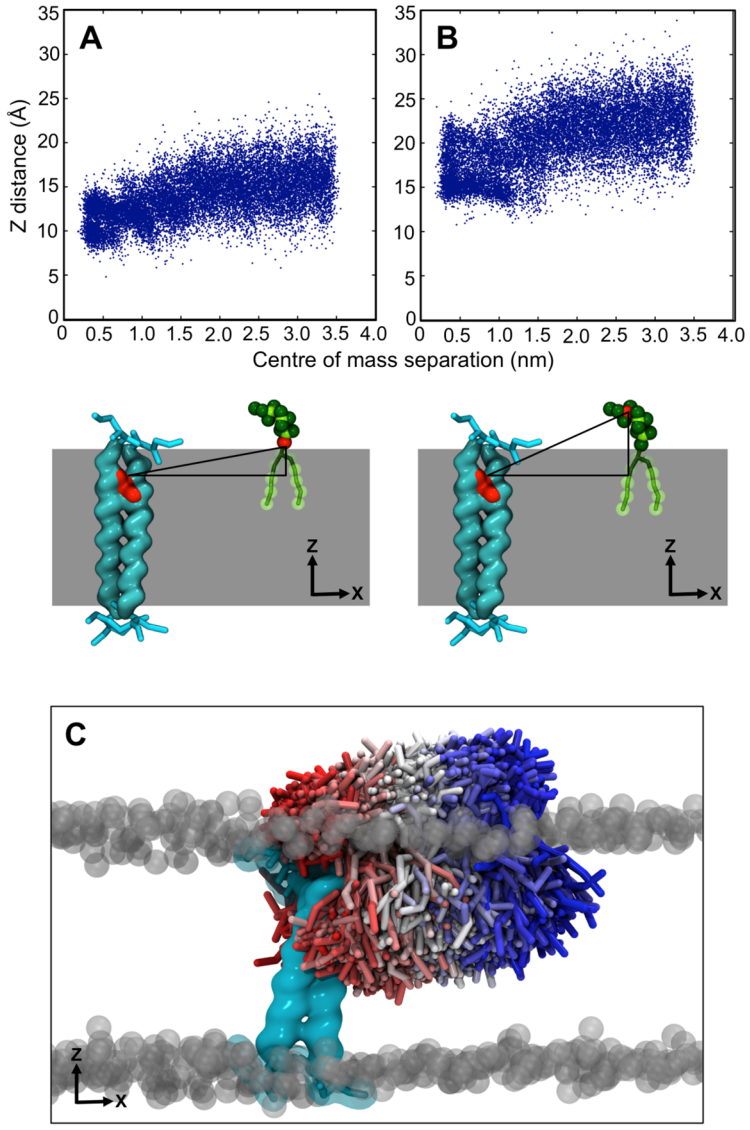

Figure S3. Relationship between GM3 Z positioning in the bilayer and lateral separation from the protein. GM3 "sinks" deeper into the bilayer in the bound state. (A+B) The z component of the relative distance between the centre-of-mass of the Gly residues within the N-terminal GxxGA dimerization motif, and the B1A (A) and INC (B) beads of GM3 over the reaction coordinate sampled during PMF calculations. Shown underneath each plot is a cartoon depicting the distance measured. The GxxGA motif and the beads used for distance calculations are indicated in red. Distances were computed for each frame of a concatenated trajectory of all windows used during calculation of the GM3 PMF profile. (C) 320 evenly distributed GM3 stick models colored by timestep from red to blue along the concatenated trajectory. The positioning of GM3 relative to the membrane surface (POPC headgroups shown as grey spheres) and the protein (cyan) can be seen to evolve over time as the lipid moves away from the protein.

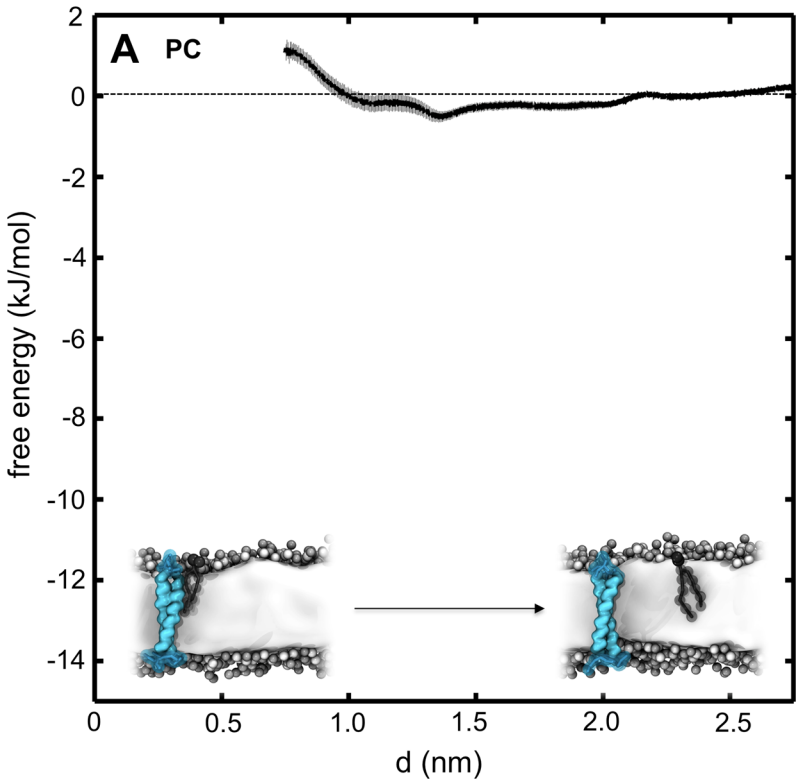

Figure S4. Outer leaflet PMF profile for PC. No significant interaction of the lipid molecule (shown in blue in the inset) with the protein (shown in cyan) of magnitude greater than kT was observed.